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) " "												
Abraham, S. A., K. Edwards, et al. "An evaluation of transmembrane ion gradient-mediated encapsulation of topotecan within liposomes." <i>J Control Release 96</i> (3): 449-61, 2004.													
	1-	 											
	AD	,		Apostolidou, E., G. Garcia-Manero, et al. "Phase I Study of OSI-211, a Novel Liposomal									
			Topoisomerase 1 (Topo 1) Inhibitor, in Patients with Refractory Leukemia." Blood, 2002.										
			· 	Abstract #4575.									
	\ AE		Biloti, D. N.,	Biloti, D. N., A. Santana Maria Helena, et al. "Lipid membrane with low proton									
			permeability.	" Biochim B	iophys Act	a 1611(1-2): 1-4, 2003.							
	AF		Bom, D., D.	P. Curran, et	al. "The n	ovel silatecan 7-tert-bu	tyldin	nethy	lsilyl-10-				
	^\		hydroxycamp	tothecin dis	plays high	lipophilicity, improved	huma	an bl	ood stabili	ty, and	1		
			potent anticar	ncer activity	." J Med C	hem 43(21): 3970-80, 2	2000.			•			
2						ighly lipophilic DNA to		mer	ase I inhib	itor DI	3-67		
	AG	ⁱ	4			uman blood and potent	-				1		
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1	AL	1				ect of composition on th							
- 1)H gradien	t method." Journal of B	lioscie	ence	and Bioen	gineeri	ing.		
		Щ.	<i>95</i> (4):405-40										
- 1	AN	,				osomal camptothecin ar							
Formulation, pharmacokinetics and preclinical anti-tumor activity." Proceedings of the													
Controlled Release Society, pp. 919-920, 1997.													
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hl	BC										
<i></i>	[liposomal delivery of 9-nitro-camptothecin." Ann NY Acad Sci 922:164-74, 2000.								
	ВД	i i	Clements, M. K., C. B. Jones, et al. "Antiangiogenic potential of camptothecin and								
			opotecan." Cancer Chemother Pharmacol 44(5): 411-6, 1999.								
- 1	BE	Clements, M	Clements, M. K., S. Wasi, et al. "Camptothecin exhibits selective cytotoxicity towards								
- 1	1 52	human breast	human breast carcinoma as compared to normal bovine endothelial cells in vitro."								
- 1		Anticancer D	rugs 7(8): 8	51-7, 1996)•				ľ		
1					Encapsulation of the to	poisom	erase Linhibi	or			
- 1	BF				H) liposomes: pharmac				ivity		
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	_				ntitumor effect of lipos						
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1	Bl	1 I			"Theoretical models fo	r drug (delivery to so	lid tum	ors."		
		Crit Rev Bion									
ł	ВЈ	Emerson, D.	L. "Liposom	al delivery	of camptothecins." Ph	armace	utical Scienc	e and			
		Technology T	<i>Foday 3</i> (6): 2	205-209, Ju	ine 2000.				J		
	חע	Emerson, D.	L., N. Amir	gahari, et a	l. "NX-211, a liposoma	l formu	lation of lurto	tecan			
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20	СС	Erickson-Mi	ller, C. L., R	. D. May, 6	et al. "Differential toxic	ity of cam	ptothecin,	topote	can		
and 9-aminocamptothecin to human, canine, and murine myeloid progenitors (CFU-GM) in											
		vitro." Cance	vitro." Cancer Chemother Pharmacol 39(5): 467-72, 1997.								
	CD		Garcia-Carbonero, R. and J.G. Supko "Current perspectives on the clinical experience,								
	"		pharmacology, and continued development of the camptothecins." Clin Cancer Res 8(3):								
	Ш	641-661, Ma									
	CE			-	e 1 study of OSI-211 gi						
1			. -	ee weeks ii	n patients with solid car	ncers." Im	vest New D	rugs 22	?(3):		
	\vdash	263-75, 2004									
- 1	CF				hase I and pharmacokin						
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		2): 85-92, 20		01p000		11,00). 0	o oao.	,	-(-		
				"Camptot	thecin delivery methods	s." Pharm	Res 19(10)	:1389-	1399.		
	CI	October 2002			,		-102 -5 (20)	,	,		
	Cì	Khan, S., A.	Ahmad, et al	l. "A sensit	tive and rapid liquid chi	romatogra	phy tanden	n mass			
	.,	spectrometry	method for a	quantitativ	e determination of 7-et	hyl-10-hy	droxycamp	totheci	n		
. ((SN-38) in h	uman plasma	containin	g liposome-based SN-3	8 (LE-SN	[38]." Biom	edical			
' chromatography - BMC 17(8): 493-9, 2003.											
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Knight V. F. S. Kleinerman, et al. "O Nitrocomptothesin linesame sergeal treatment of										
$\Delta(I)$.	DC	human cancer subcutaneous xenografts and pulmonary cancer metastases in mice." Ann N Y								
Cle 1			· · · · · · · · · · · · · · · · · · ·							
		·····	Acad Sci 922: 151-63, 2000.							
- 1	DD	_	Knight, V., N. Koshkina, et al. "Anti-cancer activity of 9-nitrocamptothecin liposome							
					matol Assoc 111: 135-4					
	DE	Knight, V., 1	N. V. Koshki	na, et al. "A	Anticancer effect of 9-n	itrocampt	othecin lip	osome		
- 1	DE	aerosol on hi	ıman cancer	xenografts	in nude mice." Cancer	Chemoth	er Pharma	col 44(3):		
		177-86, 1999		•				` '		
				lhert et al	. "Distribution of camp	tothecin a	fter deliver	v as a		
	DF				nuscular injection in m					
- 1		Pharmacol 4			nuscular injection in in	icc. Canc	er Chemoi	ner		
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- 1			and osteosa	rcoma lung	g metastases in mice." (Iin Cance	er Res 6(7)	: 2876-80,		
- $+$		2000.								
	DH				mproved respiratory de	-		•		
Į į		· camptothecia	n and paclitar	xel, with 59	% CO2-enriched air: ph	armacoki	netic studio	es." Cancer		
		Chemother F	Pharmacol 47	7(5): 451-6	, 2001.					
		Lei, S., PY.	Chien, et al.	"Enhance	d therapeutic efficacy o	f a novel	iposome-b	ased		
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1		773-8, 2004.						3, ugs 10(0).		
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1	1				y, pharmacokinetic and	merapeun	ic evaluatio	on.		
		Anticancer L								
Liu, X., B. C. Lynn, et al. "A versatile prodrug approach for liposomal core-loading of										
		water-insolul	ole camptoth	ecin antica	ncer drugs." J Am Chen	n Soc 124	(26): 7650 _:	-1, 2002.		
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Loos, W. J., D. Kehrer, et al. "Liposomal lurtotecan (NX211): determination of total drug											
levels in human plasma and urine by reversed-phase high-performance liquid											
[(XY [chromatography." J Chromatogr B 738(1): 155-63, 2000.										
	Loos, W. J., J. Verweij, et al. "Structural identification and biological activity of 7-methyl-										
1	// I MI) []										
- 1	10,11-ethylenedioxy-20(S)-camptothecin, a photodegradant of lurtotecan." Clin Cancer Res 8(3): 856-62, March 2002.										
					camptothecin derivati	voc fo		into			
- 1	EE	_ ·	_	-	ns." <i>Anticancer Drug L</i>		-				
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	Er	Yao xue xue	bao = Acta j	pharmaceu	tica Sinica 19(1): 63 <mark>-</mark> 8,	1984.		,	-		
	EG	Lynam, E., I). J. Landfair	, et al. "Ca	mptothecin analogue e	fficacy	y in vitro: Effe	ct of	•		
	EG	liposomal en	capsulation (of GI14721	1C (NX211)." Drug D	eliver	y: Journal of L	Delivery	and		
		Targeting of				•	•	•			
		MacKenzie,	M. J., H. W.	Hirte, et a	l. "A phase I study of O	SI-21	1 and cisplatin	as			
- 1	EH				1, 2 and 3 every 3 wee				cers."		
		Ann Oncol 1			,						
					n, et al. "Circumvention	of br	east cancer res	istance			
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	ll	·	•		n Cancer Res 7(4): 935		_	0102	,5 0.		
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		10(19): 6638									
Mi, Z. and T. G. Burke "Differential interactions of camptothecin lactone and carboxylate											
701111111111111	forms with human blood components." Biochemistry 33(34): 10325-36, 1994.										
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~ /	FC	P	roulx, M. F	E., A. Desorm	neaux, et a	l. "Treatment of visco	eral leishn	naniasis with	sterica	lly	
111/1	1 1	s	stabilized liposomes containing camptothecin." Antimicrob Agents Chemother 45(9): 2623-								
Cio			7, 2001.								
	FD		Proulx, M. E., J. F. Marquis, et al. "Incorporation of campthothecin into liposomes: A new								
- 1	'		approach for the treatment of leishmaniasis." Abstracts of the 39th Annual Interscience								
				on Antimicro	bial Agent	s and Chemotherapy	, San Fran	icisco, 1999.	Abstra	act	
	1		856.			·			<u> </u>		
1	FE					some and conversion	n to active	metabolite."	Curr 1	Drug	
				31-48, 2000.							
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	FH					ctive irinotecan (CP)	•	~ .		-	
			-		n to the act	tive metabolite SN-3	8." <i>Jpn J</i> (Cancer Res 90	0(2): 22	26-32,	
	<u> </u>		February 199								
	FI		-		-	phase II study of lipo		•	•		
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			_		taxel." Pro	oc Amer Assoc Cance	er Res. 41:	144, March 2	2000.		
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Tomkinson, B., R. Bendele, et al. "OSI-211, a novel liposomal topoisomerase I inhibitor, is											
14/1	active in SCID mouse models of human AML and ALL." Leukemia Research 27(11): 1039-										
w 1		50, 2003.									
I.	Verschraegen, C. F. B. E. Gilbert, et al. "Feasibility, phase I, and pharmacological study of										
I	aerosolized liposomal 9-nitro-20(S)-camptothecin in patients with advanced malignancies in										
- 1	the lungs." Ann NY Acad Sci 922: 352-4, 2000.										
					et al. "Clinical evaluation	n of the d	elivery and	safety	of		
- 1	GE				camptothecin in patient						
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					Anticancer Drugs 12(3)						
	GL				Spectrofluorimetry stud	y of intera	ction of ca	mptoth	iecin		
with liposomal bilayer." Luminescence 15:78-79, 2000.											
Bell, C. B., D. J. Landfair, et al. "Topoisomerase I (TOPO-1) modulation by liposomal											
GI147211 (NX211)." Proc Amer Assoc Cancer Res 41, p. 773, March 2000. Abstract											
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FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE ATTY, DOCKET NO. APPLICATION NO. (REV.7-80) PATENT AND TRADEMARK OFFICE 480208.407 09/896,811 APPLICANTS MATERIE DISCLOSURE STATEMENT Thomas D. Madden et al. e several sheets if necessary) FILING DATE GROUP ART UNIT June 29, 2001 1614 **U.S. PATENT DOCUMENTS** *EXAMINER FILING DATE DOCUMENT NUMBER DATE NAME CLASS SUBCLASS INITIAL IF APPROPRIATE HA OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.) Bevins, R. L., D. Bom, et al. "Tumor cell cycle disruption and apoptosis induced by DB-67, a highly lipophilic camptothecin displaying improved human blood stability." Proc Amer Assoc Cancer Res 42, p. 102, March 2001. Abstract #554. Bom, D. C., J. Zhang, et al. "The structural basis of camptothecin loading and retention in HC liposomal drug carriers." Proc Amer Assoc Cancer Res 42:374, March 2001. Abstract #2016. Burke, T. G., A. J. Chavan, et al. "Development and evaluation of a liposomal formulation of highly lipophilic 7-t-butyldimethylsilyl-10-hydroxy-camptothecin." Proc Amer Assoc Cancer Res 40, March 1999. Abstract #752. Burke, T. G., D. Subramanian, et al. "Enhanced bloodstream stability and in vitro activity of HE topotecan formulated in liposomes." Pharm Res 11(10):S-323, October 1994. Abstract # PDD 7596. Burke, T. G., S. Gao Xiang, et al. "Liposomal stabilization of the lactone ring of HF camptothecin anticancer drugs." Pharm Res 10(10):S-220, October 1993. Abstract # PDD Burke, T. G., X. Liu, et al. "A versatile pro-drug approach for the liposomal core loading of HG camptothecin anticancer drugs." Proc Amer Assoc Cancer Res 43, March 2002. Abstract Burke, T. G., Z. Mi, et al. (1994). "Liposomal formulations of camptothecins for cancer НН treatment." Abstracts of Papers American Chemical Society, In Proceedings of the 208th ACS National Meeting, Washington, DC, August 21-25, 1994. Abstract #50 Cao, Z. and C. Giovanella Beppino, "Liposomal prodrugs comprising derivatives of HI camptothecin and methods of treating cancer using these prodrugs." Official Gazette of the United States Patent and Trademark Office Patents 1256(1):372, March 2002. US Patent 6,352,996 B1. Chavan, A. J., K. A. Fraley, et al. "A comparative study of the human blood stability HJ characteristics of remote-loaded lipsomal carriers containing clinically-relevant camptothecins." Proc Amer Assoc Cancer Res 40:417, March 1999. Abstract #6019. Chen, G., A. Double John, et al. "Characterization of liposomal mimetic formulations for HK selective targeting." Pharm Res 13:S-161, September 1996. Abstract # PPDM 8345. Chen, G., W. Barry Brian, et al. "Pharmacokinetic evaluation of liposomal camptothecin." HL. Pharm Res 13(9):S-479, September 1996. **EXAMINER** DATE CONSIDERED * EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant(s).

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					Author, Title, Date, Pertinent Page							
(γ)	IC	Cherian, M.	"Lyophilizat	e of lipid c	omplex of water insolu	ble camp	tothecins."	Official				
(y)		Gazette of th	Gazette of the United States Patent and Trademark Office Patents 1269(3), April 2003.									
,		U.S. Patent 6			33		(// 1					
				****	toxicity evaluation of a	linosom	e-based for	mulation of				
	ID	· ·	•	•	•	•						
		1 1	•	ne cancer	cell lines." <i>Proc Amer A</i>	issoc Cai	ncer Kes 44	:314, July				
			2003. Abstract #1607.									
	IE	Choice, E., N	Choice, E., M. B. Bally, et al. "Delivery of topotecan using liposomes: Drug loading into									
		liposomes an	d drug and o	arrier phar	macokinetics in female	Balb/c n	nice." Proc	Amer Assoc				
		_		_								
			Cancer Res 40, March 1999. Abstract #753. Chow, D. S. L., G. Chen, et al. "Pharmacokinetics and in vivo antitumor activity of									
	IF		liposomal encapsulated camptothecin and its analog." Proc Amer Assoc Cancer Res 38,									
			March 1997.									
	-			et al. "Form	nulation study for the ar	ntitumor	drug campte	othecin:				
	IG		-		microemulsion." Int J			ı				
					somes, micelles and mi							
	IH		-	-	harm Sci 6(Supp. 1):S3,			- 1				
												
	11	Dallavalle, S., L. Merlini, et al. "Perspectives in camptothecin development." Expert Opinion on Therapeutic Patents 12(6):837-844, 2002.										
					· · · · · · · · · · · · · · · · · · ·							
	ע		Daoud, S. S., M. I. Fetouh, et al. (1993). "Multilamellar liposomes as a delivery system for									
1 1		_	camptothecin (NSC 94600) and 9-aminocamptothecin (NSC 603071)." in <i>Proc Amer Assoc</i>									
		Cancer Res.	Orlando, FL	, May 19-2	2, 1993, 367. Abstract	#2188						
	ıĸ	Desjardins, J	. P., D. L. Ei	nerson, et	al. "Biodistribution of I	VX 211,	iposomal C	I147211, in				
	IK.	tumor bearin	tumor bearing mice." Proc Amer Assoc Cancer Res 41:702, March 2000. Abstract #4467.									
	IL	Emerson, D.	L., N. Amir	ghahari, et	al. "Enhanced in vivo a	ntitumor	efficacy of	the liposome				
formulated topoisomerase I inhibitor Lurtotecan." Proc Amer Assoc Cancer Res												
	40:113,March 1999. Abstract #751											
					n vivo antitumor effica	cy of lipo	somal lurto	tecan (NX				
I [IM		-	-	ner Assoc Cancer Res 4	-		`				
		#545.				,						
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		ОТНЕ	CR PRIOR A	RT (Including	z Author, Title, Date, Pertinent Pag	ges, Etc.)					
$\overline{\Lambda}$	[Gelmon K	A. E. Eisenl	nauer, et al.	"Phase 1 study of NX	211 (linos	somal lurto	tecan) given			
- () ()	JC	-	Gelmon, K. A., E. Eisenhauer, et al. "Phase 1 study of NX 211 (liposomal lurtotecan) given								
W.			as an intravenous infusion on days 1, 2, and 3 every weeks in patients (pts) with solid								
				l trials gro	up study." <i>Proc Amer A</i>	ssoc Can	cer Res 41:	610, March			
		2000. Abstra	act #3879.								
	Į,	Gilbert, B. E	A. Servshe	v. et al. "9	-nitrocamptothecin lipo	some aer	osol: lack o	f subacute			
- 1	JD	i .	Gilbert, B. E., A. Seryshev, et al. "9-nitrocamptothecin liposome aerosol: lack of subacute toxicity in dogs." <i>Inhal Toxicol 14</i> (2): 185-97, 2002.								
						of 0 =:		hadin in			
	JE	. =			mproved lactone stabili	-	-	-			
			vitro and in vivo by liposomal formulation." Proc Amer Assoc Cancer Res 39:430, March								
		1998. Abstra			 						
	JF				ustained organ exposur						
			lactone form by liposomal delivery." Proc Amer Assoc Cancer Res 40:417, March 1999.								
			Abstract #2756.								
	JG	Gong, L., G. Chen, et al. "Development and characterization of liposomal formulation of 9									
1		nitro-campto	thecin." Pha	rm Res 13:	S-162, September 1996	6. Abstrac	ct #6021.	•			
	77.	Haas, H., B.	Haas, H., B. Schulze, et al. "Strong antitumor efficacy of a cationic liposomal camptothecin								
	Ж		formulation (LipoCamTM) in the subcutaneous human melanoma A-375 in nude mice."								
			Proc Amer Assoc Cancer Res 44:350-351, July 2003. Abstract # R1793.								
					Therapeutic efficacy of			ulation of			
	JI				D2F1 mice." Proc Amer						
					721'1 IIIICC. 170C Amer	Assoc Ci	incer Nes 4	4, 2 Eu.,			
		July 2003. A			and formulation COM	20 (1 12 0) NI20), A.C.				
	IJ		Khan, S., S. Ali, et al. "Liposome based formulation of SN-38 (LE-SN38): A four-cycle								
			toxicity evaluation in beagle dogs." Toxicological Sciences 72(S-1), March 2003. Abstract								
		#1873.									
	JK	Knight, J. V.	, B. Gilbert,	et al. "Sma	III particle liposome aer	osols for	delivery of	anti-cancer			
drugs." Official Gazette of the United States Patent and Trader							nark Office Patents				
		1236(3):2973	3, July 18, 20	000. U.S. I	Patent 6,090,407.			1			
	Koshkina, N. V., B. E. Gilbert, et al. (1999). "Pharmacokinetics and tissue distribution of										
	JL				some aerosol or follow						
l l		mice." Proc Amer Assoc Cancer Res 40:10, March 1999. Abstract #734.									
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00	,,,	Kruszewski,	S., A. S. Ch	avan, et al.	(2000). "Comparison of	f the hum	an blood c	hemistry of		
/d();	KC	free versus li	free versus liposomal forms of the clinically-relevant topoisomerase I inhibitor Lurtotecan							
W		(GI147221).'	Proc Amer	Assoc Can	ncer Res 41:324, March	2000. At	stract #20	56.		
	KD				umor agents." Idrugs 20					
	,,,	Loos, W. J.,	D. F. S. Keh	rer, et al. "	Clinical pharmacodyna	mics of lip	osomal lu	rtotecan (NX		
	KE				natologic toxicity." Pro					
1		, ,	42:102, March 2001. Abstract #551.							
					l. "The novel highly lip	ophilic to	noisomera	se I inhibitor		
	KF			•	~	-	•	t		
		DB67 is effective in the treatment of liver metastases of murine CT-26 colorectal carcinoma." <i>Proc Amer Assoc Cancer Res</i> 44(2): 348, 2003. Abstract #1782.								
								rt of		
	KG		Lynam, E., D. J. Landfair, et al. "Camptothecin analogue efficacy in vitro: Effect of liposomal encapsulated of GI147211C (Lurtotecan) on vitro cytotoxicity for multiple tumor							
					r Res 31:421, March 19		city for int	intiple tullor		
	-				"Liposome-based appro		01/0700700	ontionnon		
	КН	1		-	* **		overcome	anticancer		
					pdates 6:271-279, 2003			·		
	ΚI	Michaelis, U., B. Schulze, et al. "Cationic liposomes (Catioms) to target tumor								
		neovasculature." Abstracts of Papers American Chemical Society, in <i>Proceedings of the</i> 226 th ASC National Meeting, New York, September 7-11, 2003.								
	ĸЈ	Moynihan Karen, L., L. Emerson David, et al. "Liposomal camptothecin formulations."								
		Official Gazette of the United States Patent and Trademark Office Patents, 2004. U.S.								
		Patent 6,740,								
	KK		Pal, A., S. Sheikh, et al. "Enhanced antitumor efficacy of liposome-based formulation of							
	I KK	SN38 against human pancreatic tumor in SCID mice." Proc Amer Assoc Cancer Res, 2003.								
		Abstract #1785.								
	KL	Poirot, K., Y	Poirot, K., Y. Zou, et al. "Liposomal-camptothecin composed of cationic phospholipids							
	\r\	containing ur	containing unsaturated fatty acids: Formulation and cytotoxicity studies." Proc Amer Assoc							
		Cancer Res 37:300, March 1996. Abstract #2039.								
	,,,				tumor effect of CPT-11	encapsula	ated liposo	me and		
•	conversion to active metabolite." J Liposome Res, pp. 101-102, 1998.									
EXAMINE	R				DATE CONSIDERED		, /			
		Le 15		<u></u>]		71	20/0	25		
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		ОТНЕ	R PRIOR AR	T (Including	g Author, Title, Date, Pertinent Pa	ges, Etc.)				
10 i	ιc	Sarkar, A., N	. Kamath, et a	al. "Toxic	city evaluation of a lipos	some-	base	d formulat	ion of	SN38	
al		in mice." Tox	cicol Sci 72(S-	-1):83, M	farch 2003. Abstract #403.						
		Semple, S. C	Semple, S. C., B. L. S. Mui, et al. "Comparative efficacy and therapeutic index of topotecan								
	LD										
		,	and liposomal topotecan in murine and human solid tumor models." <i>Proc Amer Assoc Cancer Res 44</i> , July 2003. Abstract #3658.								
				· ·							
	LE	_			Pre-clinical evaluation	-		_			
			efficacy and therapeutic index in murine and human xenograft tumor models compared to								
		free drug." P.	roc Amer Asso	oc Cance	r Res 42:374, March 20	001. <i>A</i>	Abstr	act #2015.	<u> </u>		
	LF	Sugarman, S	and R. Perez	-Soler "L	iposomal camptothecin	: For	nula	tion and cy	totoxic	city	
		against KB c	against KB cells." Proc Amer Assoc Cancer Res, Orlando, FL, May 19-22, 1993,p. 422.								
		Abstract #25	19.						_		
	LG	Tanyeli, C., I	D. Bom, et al.	"Formula	lation and pharmacological characterization of the novel						
	ш	polyamine ca	mptothecin C	T-17 enc	17 encapsulated in low-clearance liposomes." Proc Amer Assoc						
			Cancer Res 42:255, March 2001. Abstract #1379.								
			-,,,		01). "Efficacy of NX 2	11 in :	SCIL) mouse m	odels o	f	
	LH			-	•	12:100, 2001. Abstract #542.					
					ed release of topotecan				linoso	mes "	
	LI		• .		8, March 1995. Abstra			11030113141 * (npose	mics.	
								acec entitue	mor off		
	n	· ·	•		ALTH liposome formulation enhances antitumor efficacy						
		· · · · · · · · · · · · · · · · · · ·	•		hibitor, in human tumor xenograft models." <i>Proc Amer</i>						
					004. Abstract #3069.		. 0 7				
	LK			-	hecins in clinical develo	pmer	it." E	xpert Opu	i Invest	tig	
	Drugs 13(3): 269-284, 2004.										
	LL				f Topotecan in Lipid-Ba						
			of Drug Stability and Plasma Elimination in a Murine Model, and Comparison of Antitumor								
Efficacy Against Murine L1210 and B16", Proceedings from 34th Annual ASCO Meeting,											
\ 1998. Abstract #754.											
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